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Mouse PAR34 mature VH amino acid sequence (SEQ ID NO:2)

E	I	Q	L	Q	Q	S	G	P	E	L	V	K	P	G	A	S	V	K	V
S	C	K	A	S	G	Y	A	F	T	N	Y	N	M	Y	W	V	K	Q	S
H	G	K	S	L	E	W	I	G	Y	I	D	P	Y	Y	G	D	P	G	Y
S	Q	K	F	K	G	K	A	T	L	T	V	D	K	S	S	S	T	A	Y
M	H	L	N	S	L	T	S	E	D	S	A	V	Y	Y	C	A	R	R	G
N	F	P	Y	Y	F	D	Y	W	G	Q	G	T	T	L	T	V	S	S	

Mouse PAR34 mature VL amino acid sequence (SEQ ID NO:3)

D	I	K	M	T	Q	S	P	S	S	M	Y	A	S	L	G	E	R	V	T
I	T	C	K	A	S	Q	D	I	N	S	Y	L	S	W	F	Q	Q	K	P
G	K	S	P	K	T	L	I	Y	R	A	N	R	L	V	D	G	V	P	S
R	F	S	G	S	G	S	G	Q	D	Y	S	L	T	I	S	S	L	E	Y
E	D	M	G	I	Y	Y	C	L	Q	Y	D	E	F	P	Y	T	F	G	G
G	T	K	L	E	I	K													

Mouse PAR80 mature VH Region Amino Acid Sequence (SEQ ID NO:4)

E	V	Q	L	Q	Q	S	G	A	E	L	V	R	S	G	A	S	V	K	L
S	C	T	A	S	G	F	N	I	K	D	Y	Y	I	H	W	V	K	Q	R
P	E	Q	G	L	E	W	I	G	C	I	D	P	E	N	G	D	T	E	Y
A	P	N	F	Q	G	R	A	T	M	T	A	D	T	S	S	N	T	A	Y
L	Q	L	S	S	L	T	S	E	D	T	A	V	Y	Y	C	Y	G	G	T
I	T	F	A	Y		W	G	Q	G	T	L	V	T	V	S	A			

Mouse PAR80 mature VL Region Amino Acid Sequence (SEQ ID NO: 5)

Q	A	V	V	T	Q	E	S	A	L	T	T	S	P	G	E	T	V	T	L
T	C	R	S	S	T	G	A	V	T	T	S	N	S	A	N	W	V	Q	E
K	P	D	H	L	F	T	G	L	I	G	G	T	I	N	R	V	P	G	V
P	A	R	F	S	G	S	L	I	G	D	K	A	A	L	T	I	T	G	A
Q	T	E	D	E	A	I	Y	F	C	A	L	W	Y	S	N	H	W	V	F
G	G	G	T	K	L	T	V	L	G										

The CDRs based on the definition of Kabat are bolded and underlined.

FIG. 1

Panel of Monoclonal Antibodies Generated Against Human AR

ANTI-BODY	ISO-TYPE	BINDING					INHIBITION OF AR-MEDIATED PROLIFERATION (μg/ml)		
		INHIBITION OF AR-EGFR					3T3		HEKn
		AR	Surface AR	EGF	HB EGF	Cyno AR	Murine AR	IC50%	IC90%
PAR2	IgG1, λ	+++	+++	-	-	+++	+++	0.13	1.3
PAR5	IgG1, λ	+++	+++	-	-	ND	+++	0.8	7.2
PAR15	IgG1, λ	+++	++	-	-	+++	+++	0.11	0.71
PAR19	IgG2b, κ	+++	+++	-	-	ND	-	5.9	>10
PAR22	IgG1, λ	+++	++	-	-	ND	+++	6.8	>10
PAR23	IgG1, λ	+++	++	-	-	ND	++	1.7	6.9
PAR26	IgG2b, κ	+++	+++	-	-	ND	-	>10	>10
PAR29	IgG1, λ	+++	+++	-	-	ND	+++	0.9	>10
PAR31	IgG2b, λ	+++	+++	-	-	+++	+++	0.7	1.9
PAR34	IgG2b, κ	+++	+++	-	-	+++	+++	0.072	0.71
PAR44	IgG1, κ	+++	++	-	-	ND	+++	4.1	>10
PAR46	IgG1, κ	+++	++	-	-	ND	+++	0.6	>10
PAR51	IgG1, λ	+++	++	-	-	ND	++	ND	ND
PAR67	IgG2b, κ	+++	++	-	-	+++	-	ND	>10
PAR79	IgG1, κ	+++	++	-	-	ND	-	4	>10
PAR80	IgG2a, λ	+++	+++	-	-	+++	-	ND	>10
PAR81	IgG1, κ	+++	++	-	-	ND	-	ND	ND
PAR84	IgG2a, λ	+++	+++	-	-	+++	-	ND	0.51

BINDING – direct binding as detected by ELISA

INHIBITION OF AR-EGFR INTERACTION – ability to inhibit AR binding to A431 (human EGFR+ epidermoid carcinoma)

INHIBITION of PROLIFERATION – inhibition of proliferation of 3T3 (murine) cells to 100 ng exogenous human AR, or HEKn (human) cells to endogenously produced AR

ND – not determined; IC50% is the amount of the antibody needed to accomplish 50% inhibition; IC90% is the amount of the antibody needed to accomplish 90% inhibition

FIG. 2

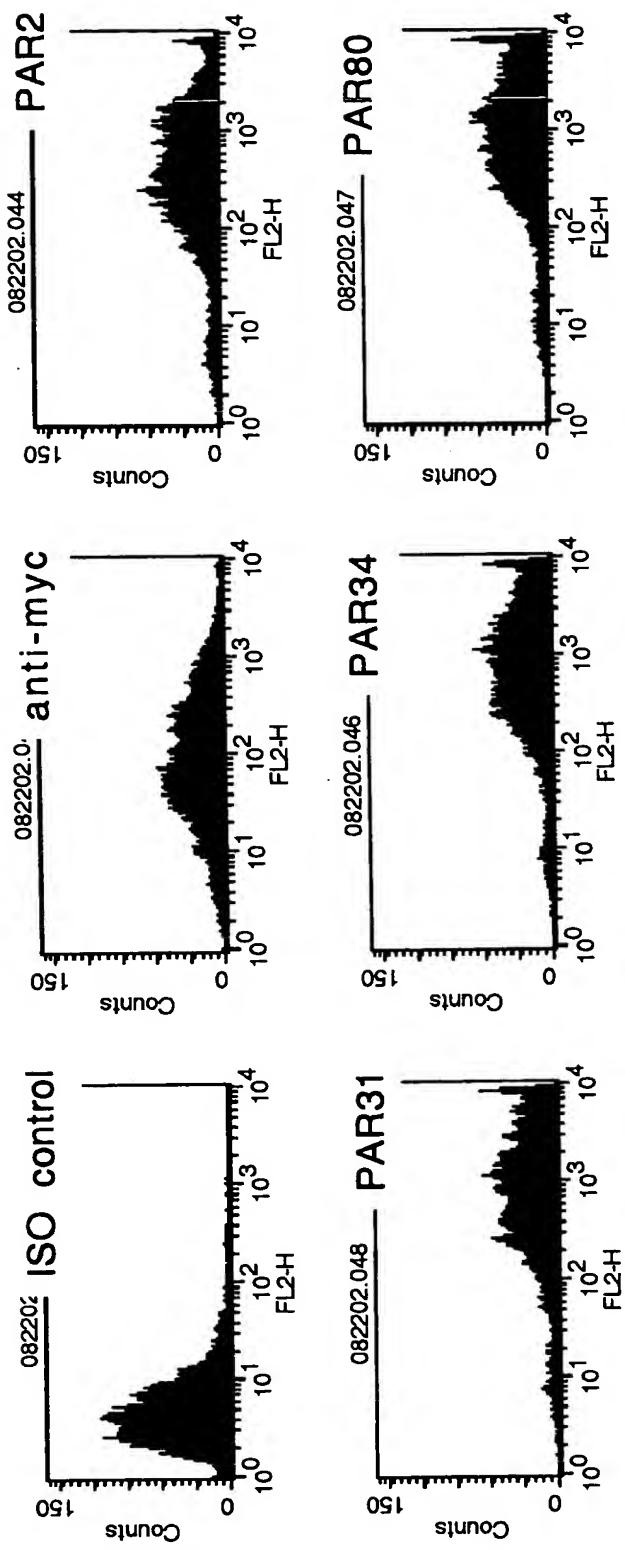


FIG. 3

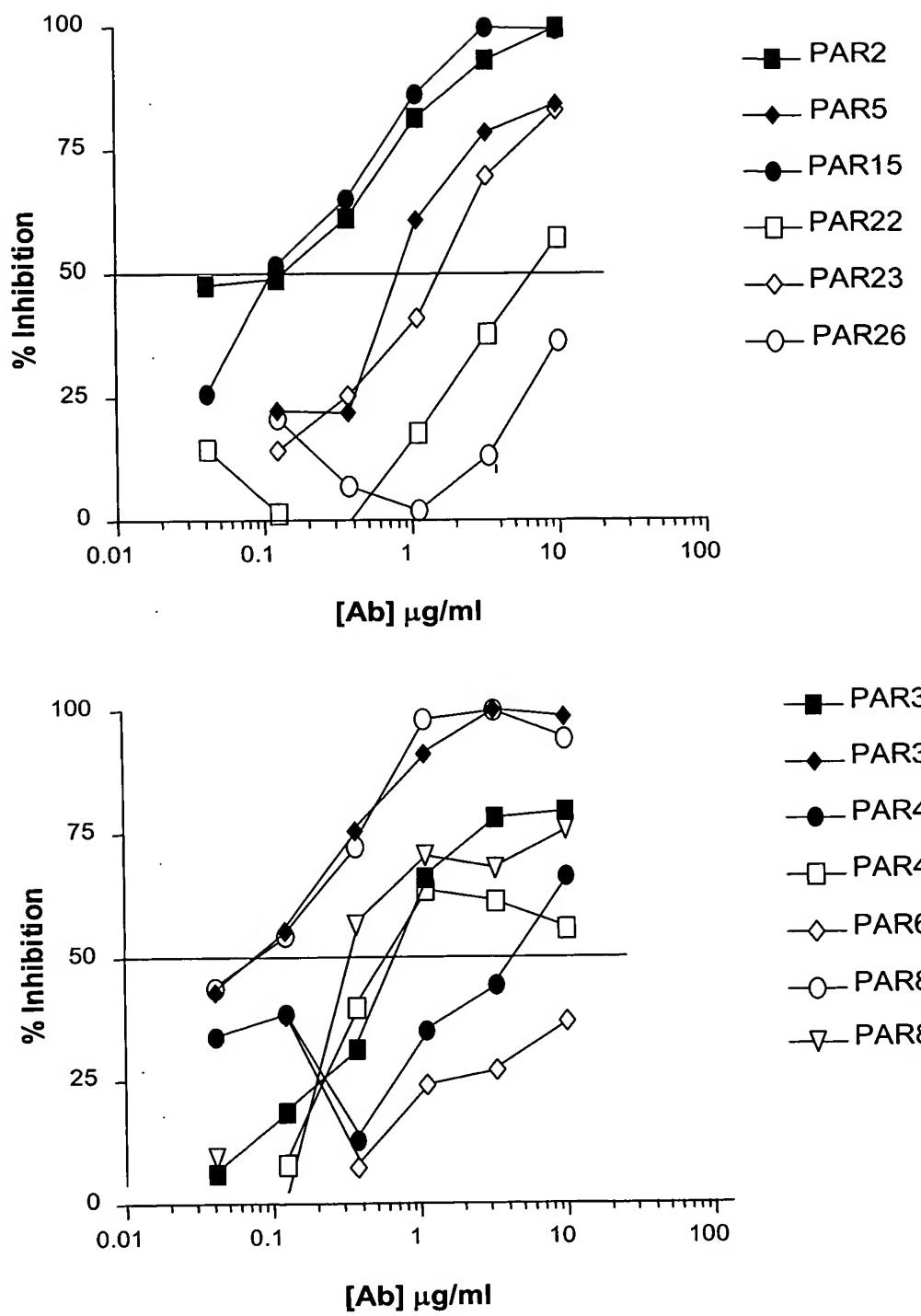


FIG. 4

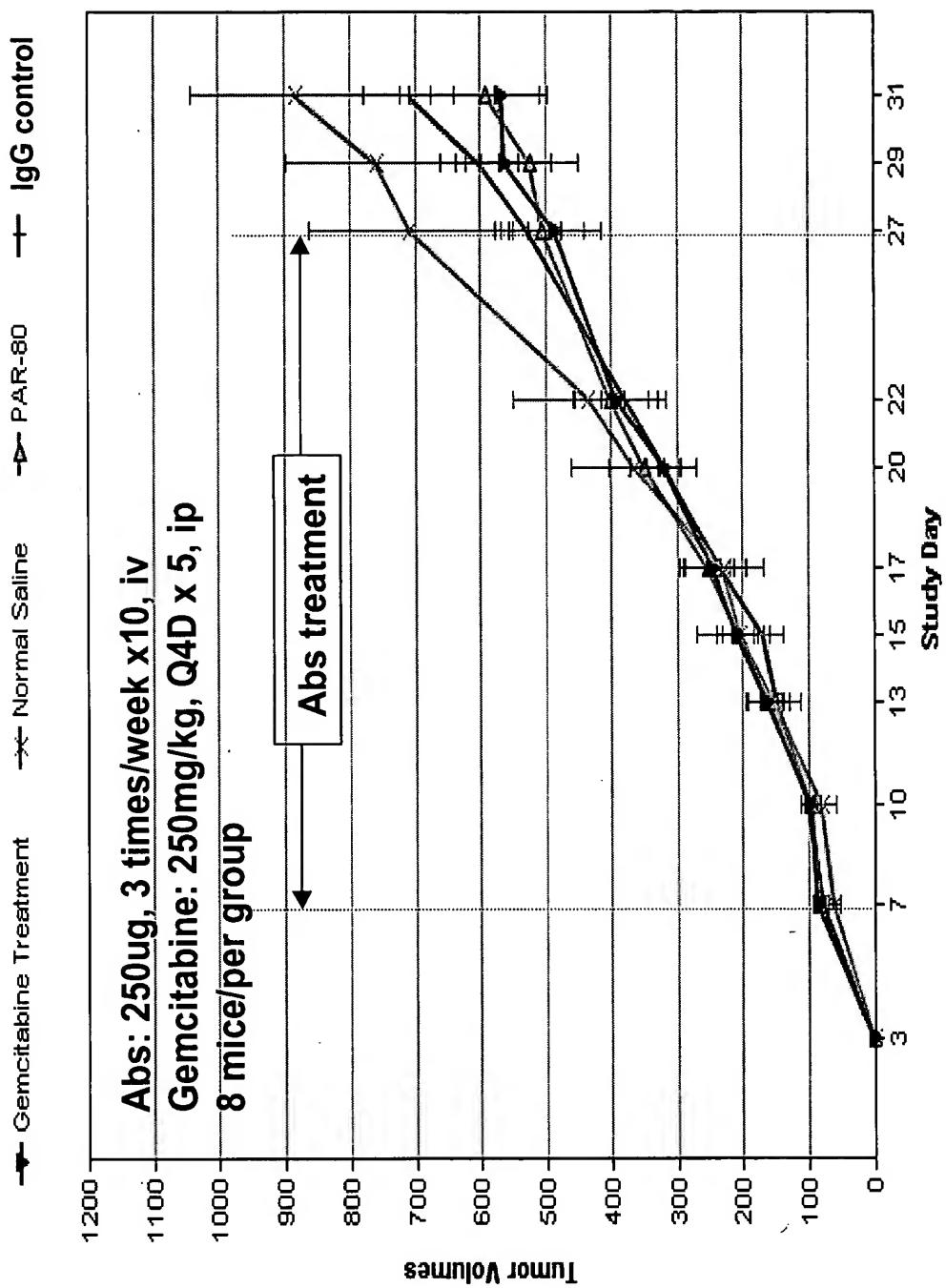


FIG. 5

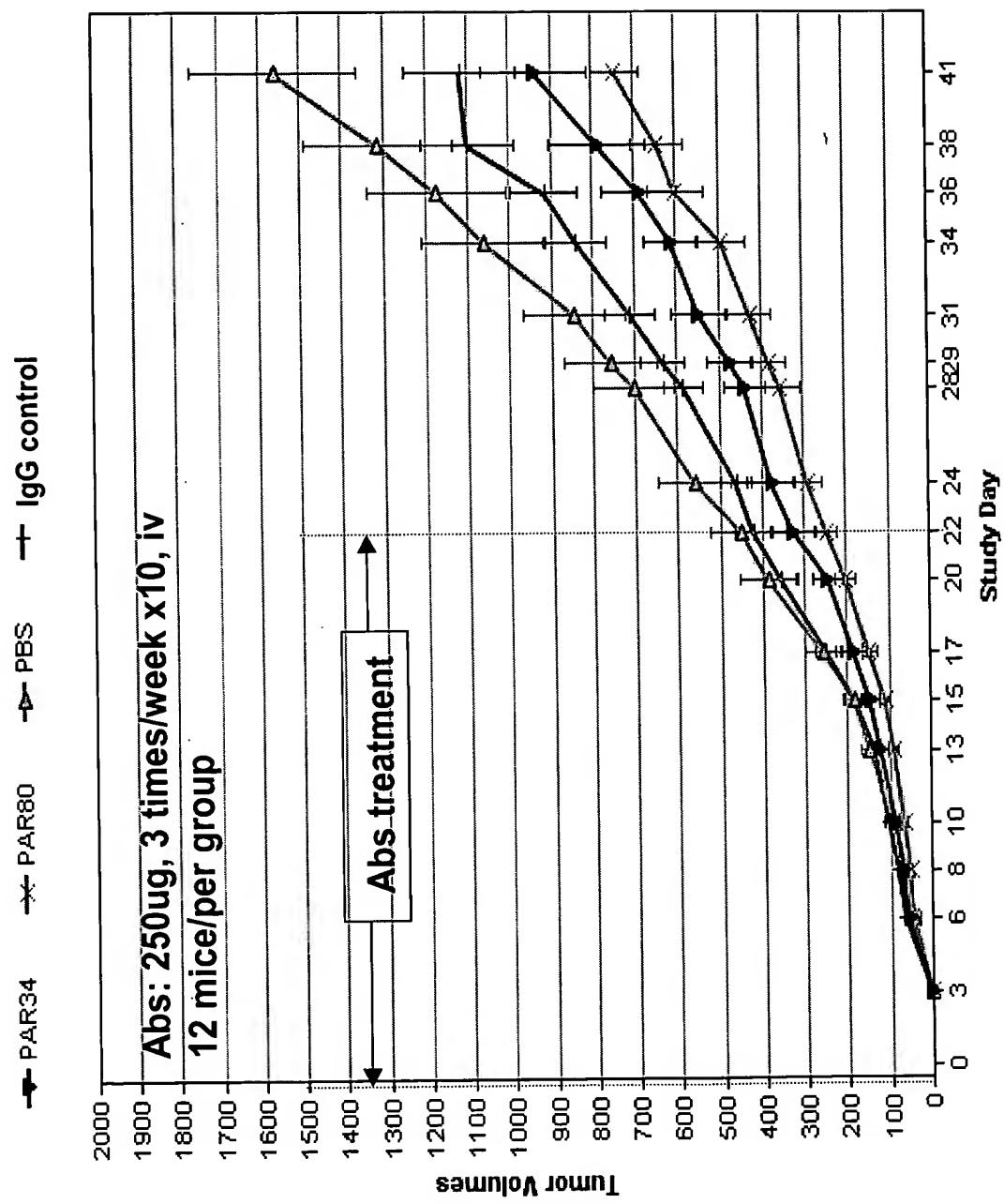


FIG. 6

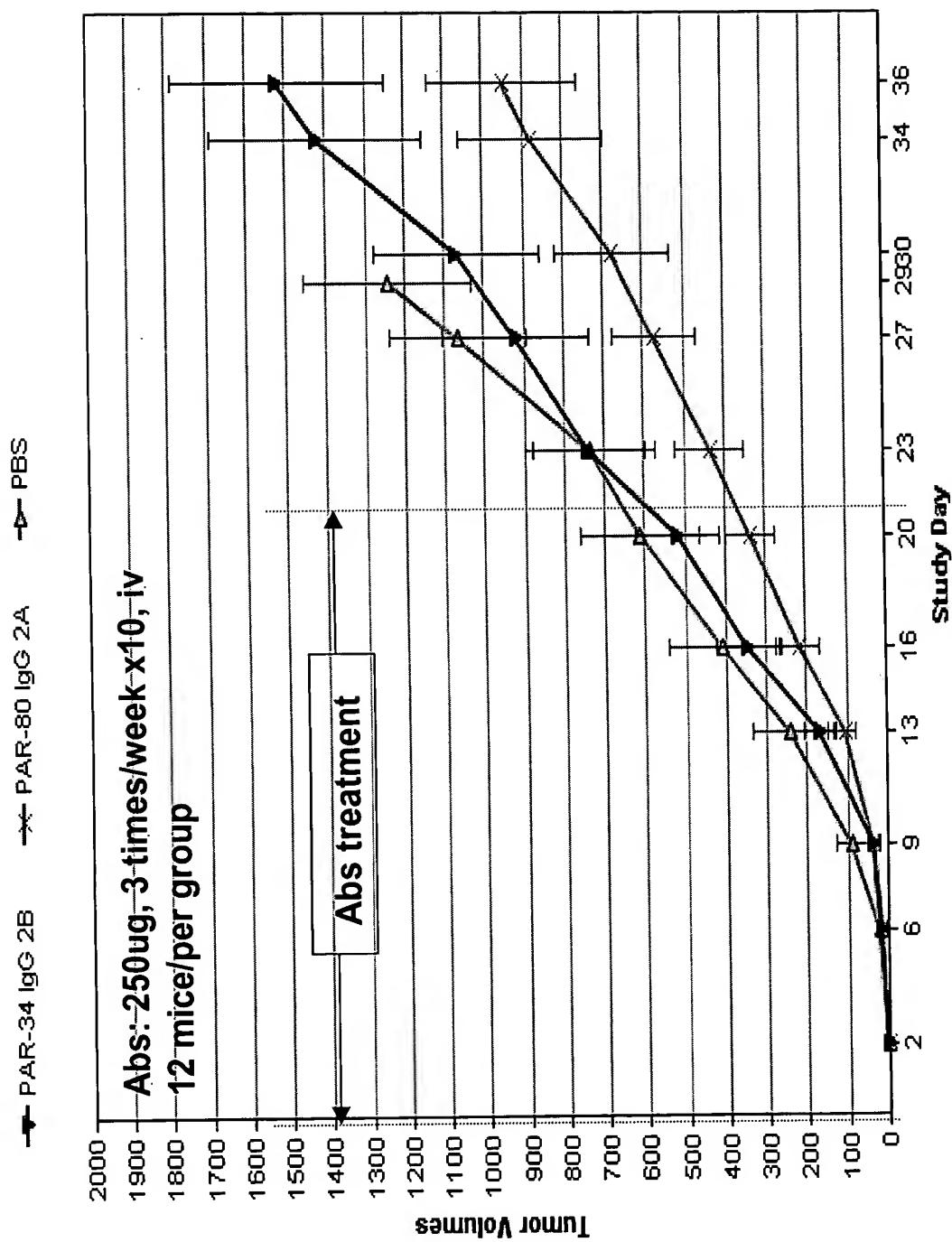


FIG. 7

cDNA (SEQ ID NO:8) and amino acid (SEQ ID NO:9) sequences for the signal peptide and heavy chain variable region of the PAR34 antibody.

30 60
ATGGAATGGAGATGGATCTTCTTCCTCTGTCAAGAACTACAGGTGTCCACTCTGAG
M E W R W I F L F L L S G T T G V H S E

90 120
ATCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGCTTCAGTGAAGGTATCC
I Q L Q Q S G P E L V K P G A S V K V S

150 180
TGCAAGGCTTCTGGTTATGCATTCACTAACATGACTGGGTGAAGCAGAGCCAT
C K A S G Y A F T N Y N M Y W V K Q S H

210 240
GGAAAGAGCCTTGAGTGGATTGGATATATTGATCCTTACTATGGTGATCCTGGCTACAGC
G K S L E W I G Y I D P Y Y G D P G Y S

270 300
CAGAAGTTCAAGGGCAAGGCCACATTGACTGTTGACAAGTCCTCCAGCACAGCCTACATG
Q K F K G K A T L T V D K S S S T A Y M

330 360
CATCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGACGGGTAAC
H L N S L T S E D S A V Y Y C A R R G N

390 414
TTCCCGTACTACTTGAATCTGGGCCAAGGCACCACTCTCACAGTCTCCTCA
F P Y Y F D Y W G Q G T T L T V S S

FIG. 8

cDNA (SEQ ID NO:10) and amino acid (SEQ ID NO:11) sequences for the signal peptide and light chain variable region of the PAR34 antibody.

30 ATGAGGACCCCTGCTCAGTTCTTGGAAATCTTGGTCTGGTTCCAGGTATCAAATGT
 M R T P A Q F L G I L L L W F P G I K C
 90 GACATCAAGATGACCCAGTCTCCATCTTCCATGTATGCATCTCTAGGAGAGAGAGACT
D I K M T Q S P S S M Y A S L G E R V T
 150 ATCACTTGCAAGGCGAGTCAGGACATTAATAGCTATTAAGCTGGTCCAGCAGAAACCA
 I T C K A S Q D I N S Y L S W F Q Q K P
 210 GGGAAATCTCCTAAGACCCCTGATCTATCGTCAAACAGATTGGTAGATGGGTCCCATCA
 G K S P K T L I Y R A N R L V D G V P S
 270 AGGTTCACTGGCAGTGGATCTGGCAAGATTATTCTCTCACCATCAGCAGCCTGGAGTAT
 R F S G S G S G Q D Y S L T I S S L E Y
 330 GAAGATATGGGAATTATTATTGTCTACAGTATGATGAGTTCCGTACACGTTGGAGGG
 E D M G I Y Y C L Q Y D E F P Y T F G G
 381 GGGACCAAGCTGGAAATAAAA
 G T K L E I K

FIG. 9

Alignment of the VH region amino acid sequences of PAR34 (SEQ ID NO:2), HuPAR34 (SEQ ID NO:12), and the human germline DP-3/JH4 segments (SEQ ID NO:13).

PAR34	E I Q L Q Q S G P E L V K P G A S V K V S C K A S G Y A F T	30
HuPAR34	E V Q L V Q S G A E V K K P G A <u>S</u> V K I S C K V S G Y <u>A</u> F T	
DP-3	E V Q L V Q S G A E V K K P G A T V K I S C K V S G Y T F T	
PAR34	N Y N M Y W V K Q S H G K S L E W I G Y I D P Y Y G D P G Y	60
HuPAR34	<u>N Y N M Y</u> W V <u>R</u> Q A P G K G L E W <u>I</u> G Y I D P Y Y G D P G Y	
DP-3	- - - - - W V Q Q A P G K G L E W M G - - - - -	
PAR34	S Q K F K G K A T L T V D K S S S T A Y M H L N S L T S E D	90
HuPAR34	<u>S Q K F K G</u> K A T L T V D K S T <u>S</u> T A Y M E L S S L R S E D	
DP-3	- - - - - R V T I T A D T S T D T A Y M E L S S L R S E D	
PAR34	S A V Y Y C A R R G N F P Y Y F D Y W G Q G T T L T V S S	119
HuPAR34	T A V Y Y C A R <u>R</u> R G N F P Y Y F D Y W G Q G T L V T V S S	
DP-3/JH4	T A V Y Y C A T - - - - - W G Q G T L V T V S S	

FIG. 10

Alignment of the VL region amino acid sequences of PAR34 (SEQ ID NO:3), HuPAR34 (SEQ ID NO:14), and the human germline L1 and JK4 segments (SEQ ID NO:15).

PAR34	D I K M T Q S P S S M Y A S L G E R V T I T C <u>K A S Q D I N</u>	30
HuPAR34	D I Q M T Q S P S S L S A S V G D R V T I T C <u>K A S Q D I N</u>	
L1	D I Q M T Q S P S S L S A S V G D R V T I T C - - - - -	
PAR34	<u>S Y L S</u> W F Q Q K P G K S P K T L I Y <u>R A N R L V D</u> G V P S	60
HuPAR34	<u>S Y L S</u> W F Q Q K P G K A P K T L I Y <u>R A N R L V D</u> G V P S	
L1	- - - W F Q Q K P G K A P K S L I Y - - - - - G V P S	
PAR34	R F S G S G S G Q D Y S L T I S S L E Y E D M G I Y Y C <u>L Q</u>	90
HuPAR34	R F S G S G S G Q D Y T L T I S S L Q P E D F A T Y Y C <u>L Q</u>	
L1	R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C - -	
PAR34	<u>Y D E F P Y T</u> F G G G T K L E I K	107
HuPAR34	<u>Y D E F P Y T</u> F G G G T K V E I K	
JK4	- - - - - F G G G T K V E I K	

FIG. 11

Nucleotide sequence (SEQ ID NO:16) and deduced amino acid sequence (SEQ ID NO:17) of the heavy chain variable region (including the signal peptide sequence) of HuPAR34 in the mini exon.

30	60
ACCGGTCCACCATGGAATGGAGATGGATCTTCTCTTCCTCTGTCAGGAAC	TACAGGTG
M E W R W I F L F L L S G T T G	
90	120
TCCACTCTGAGGTCCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGC	CTGGGGCTTC
V H S <u>E</u> V Q L V Q S G A E V K K P G A S	
150	180
TGAAAATATCCTGCAAGGTTCTGGTTATGCATTCACTAACTACAA	CATGTATTGGGTGA
V K I S C K V S G Y A F T <u>N</u> Y N M <u>Y</u> W V	
210	240
GGCAGGCCCTGAAAGGGCCTTGAGTGGATTGGATATATTGATC	CTTACTATGGTGATC
R Q A P G K G L E W I G <u>Y</u> I D P Y Y G D	
270	300
CTGGCTACAGCCAGAAGTTCAAGGGCAAGGCCACATTGACTGTTGAC	AAGTCCACCAGCA
P G Y S Q K F K G K A T L T V D K S T S	
330	360
CAGCCTACATGGAGCTCAGCAGCCTGAGGTCTGAGGACACTGCAG	TCTATTACTGTGCAA
T A Y M E L S S L R S E D T A V Y Y C A	
390	420
GACGTGGCAACTTCCGTACTACTTGACTACTGGGCCAAGGCACC	TTGTCACAGTCT
R R G N F P Y Y F D Y W G Q G T L V T V	
448	
CATCAGGTGAGTCCTCACAAACCTCTAGA	
S S	

FIG. 12

Nucleotide sequence (SEQ ID NO:18) and deduced amino acid sequence (SEQ ID NO:19) of the light chain variable region (including the signal peptide sequence) of HuPAR34 in the mini exon.

30	60
ACCGGTCCACCATGAGGACCCCTGCTCAGTTCTTGGTATCTTGGCTCTGGTTCC	
M R T P A Q F L G I L L W F P	
90	120
GTATCAAATGTGACATCCAGATGACCCAGTCTCCATCTCCCTGTCTGCATCTGGAG	
G I K C <u>D</u> I Q M T Q S P S S L S A S V G	
150	180
ACAGGGTCACTATCACTTGCAAAGCAAGTCAGGACATTAATAGCTATTAAGCTGGTCC	
D R V T I T C <u>K A S Q D I N S Y L S W F</u>	
210	240
AGCAGAAACCAGGGAAAGCTCCTAACAGACCCCTGATCTATCGTCAAACAGATTGGTAGATG	
Q Q K P G K A P K T L I Y <u>R A N R L V D</u>	
270	300
GGGTCCCCTCAAGATTCAAGTGGCAGTGGATCTGGCAAGATTATACTCTCACCATCAGTA	
G V P S R F S G S G S Q D Y T L T I S	
330	360
GCCTGCAGCCTGAGGATTCGCAACTTATTATTGTCTACAGTATGAGTTCCGTACA	
S L Q P E D F A T Y Y C <u>L Q Y D E F P Y</u>	
390	415
CGTTCGGAGGAGGGACCAAGGTGGAAATAAACGTAAGTGCACCTTCCTCTAGA	
<u>T F G G G T K V E I K</u>	

FIG. 13

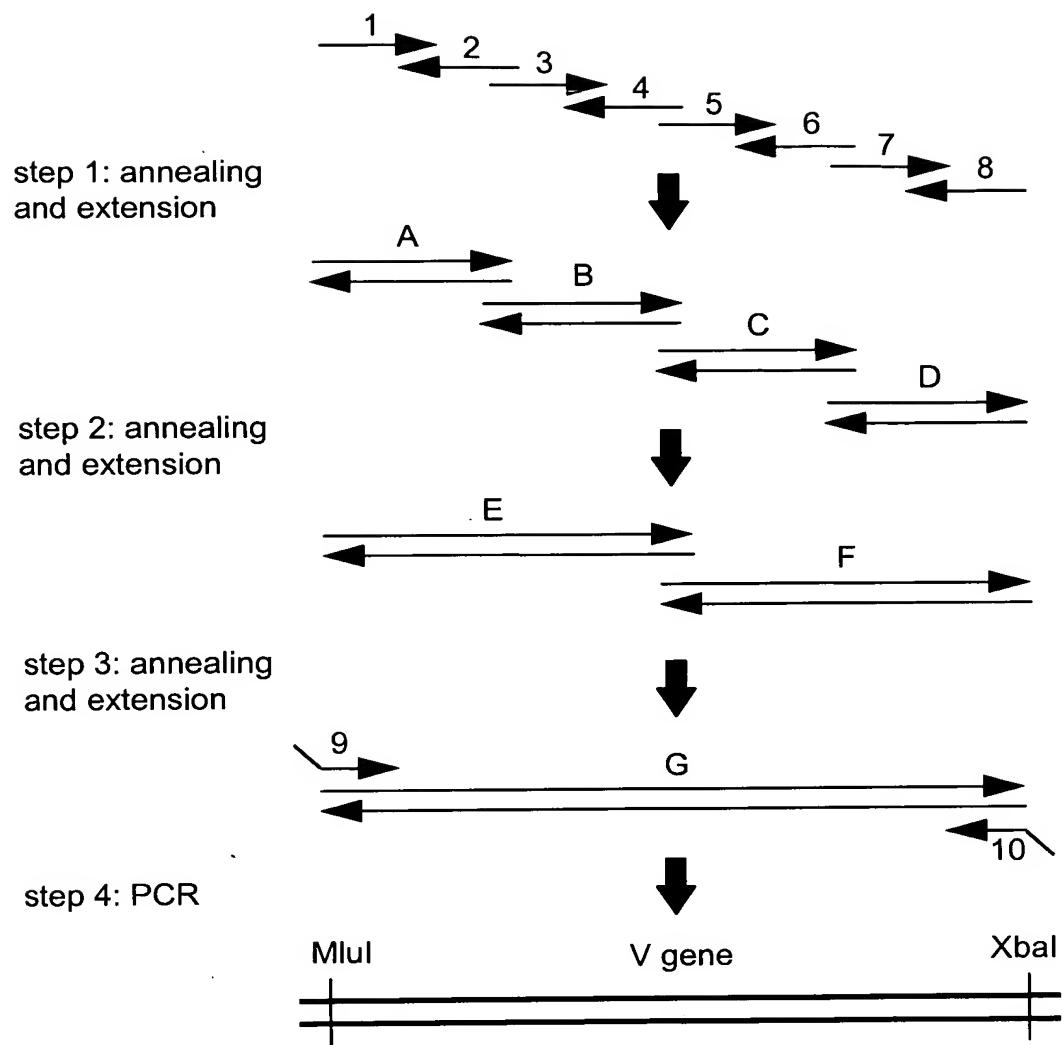


FIG. 14

Oligonucleotide primers used for the synthesis of the HuPAR34 VH gene.

Oligonucleotide 1 (SEQ ID NO:20)

5'-CTAGCCACCGCGTCCACCATGGAATGGAGATGGATCTTCTCTCCTGTCAAGGAACCTACAGGTGTCCACTCTG-3'

Oligonucleotide 2 (SEQ ID NO:21)

5'-TTCACAGAAGCCCCAGGCTTCTTCACCTCAGCTCCAGACTGCACCACTGGACCTCAGAGTGGACACCTGTAGTTCC-3'

Oligonucleotide 3 (SEQ ID NO:22)

5'-AAGCCTGGGGCTCTGTGAAAATATCCTGCAAGGTTCTGGTTATGCATTCAACTACAACATGTATTGGGTG-3'

Oligonucleotide 4 (SEQ ID NO:23)

5'-CCATAGTAAGGATCAATATATCCAATCCACTCAAGGCCCTTCCAGGGCCTGCCTCACCCAATACATGTTGTAGTTAG-3'

Oligonucleotide 5 (SEQ ID NO:24)

5'-GGATATATTGATCCTACTATGGTGATCCTGGCTACAGCCAGAAGTTCAAGGGCAAGGCCACATTGAC-3'

Oligonucleotide 6 (SEQ ID NO:25)

5'-TGCCTCAGACCTCAGGCTGCTGAGCTCCATGTAGGCTGTGCTGGACTGTCAACAGTCAATGTGGCCTTGCCCTG-3'

Oligonucleotide 7 (SEQ ID NO:26)

5'-GCAGCCTGAGGTCTGAGGACACTGCAGTCTATTACTGTGCAAGACGTGGCAACTTCCGTACTACTTGACTACTGGGG-3'

Oligonucleotide 8 (SEQ ID NO:27)

5'-GACTCGCTAGAGGTTGTGAGGACTCACCTGATGAGACTGTGACAAGGGTGCCTGGCCCCAGTAGTCAAAGTAGTACG-3'

Oligonucleotide 9 (SEQ ID NO:28)

5'-CTAGCCACCGCGTCCACCATG-3'

Oligonucleotide 10 (SEQ ID NO:29)

5'-GACTCGCTAGAGGTTGTGAG-3'

FIG. 15

Oligonucleotide primers used for the synthesis of the HuPAR34 VL gene.

Oligonucleotide 1 (SEQ ID NO:30)

5'-CTAGCCACCGCGTCCACCATGAGGACCCCTGCTCAGTTCTTGGTATCTTGGCTCTGGTTCCGGTATC-3'

Oligonucleotide 2 (SEQ ID NO:31)

5'-CAACAGATGCAGACAGGGAAAGATGGAGACTGGGTACATCTGGATGTCACATTGATACCAGGAAACCAGAGCAAC-3'

Oligonucleotide 3 (SEQ ID NO:32)

5'-CTTCCCTGTCTGCATCTGTTGGAGACAGGGTCACTATCACTTGCAAAGCAAGTCAGGACATTAATAGC-3'

Oligonucleotide 4 (SEQ ID NO:33)

5'-GATCAGGGTCTTAGGAGCTTCCCTGGTTCTGCTGGAACCAGCTTAAATAGCTATTAATGTCCTGACTTGC-3'

Oligonucleotide 5 (SEQ ID NO:34)

5'-GAAAGCTCTAACGACCCGTATCGTGCACACAGATTGGTAGATGGGTCCCATCAAGATTCAAGTGGCAGTGGATC-3'

Oligonucleotide 6 (SEQ ID NO:35)

5'-CCTCAGGCTGCAGGCTACTGATGGTAGAGTATAATCTGCCAGATCCACTGCCACTGAATCTTG-3'

Oligonucleotide 7 (SEQ ID NO:36)

5'-CAGTAGCCTGCAGCCTGAGGATTCGCAACTTATTATTGTCTACAGTATGATGAGTTCCGTACACGTTGGAGG-3'

Oligonucleotide 8 (SEQ ID NO:37)

5'-GACTCGTCTAGAAGGAAAGTGCACTTACGTTTATTCCACCTTGGTCCCTCCGAAACGTGTACGGAAAC-3'

Oligonucleotide 9 (SEQ ID NO:38)

5'-CTAGCCACCGCGTCCACCATG-3'

Oligonucleotide 10 (SEQ ID NO:39)

5'-GACTCGTCTAGAAGGAAAG-3'

FIG. 16

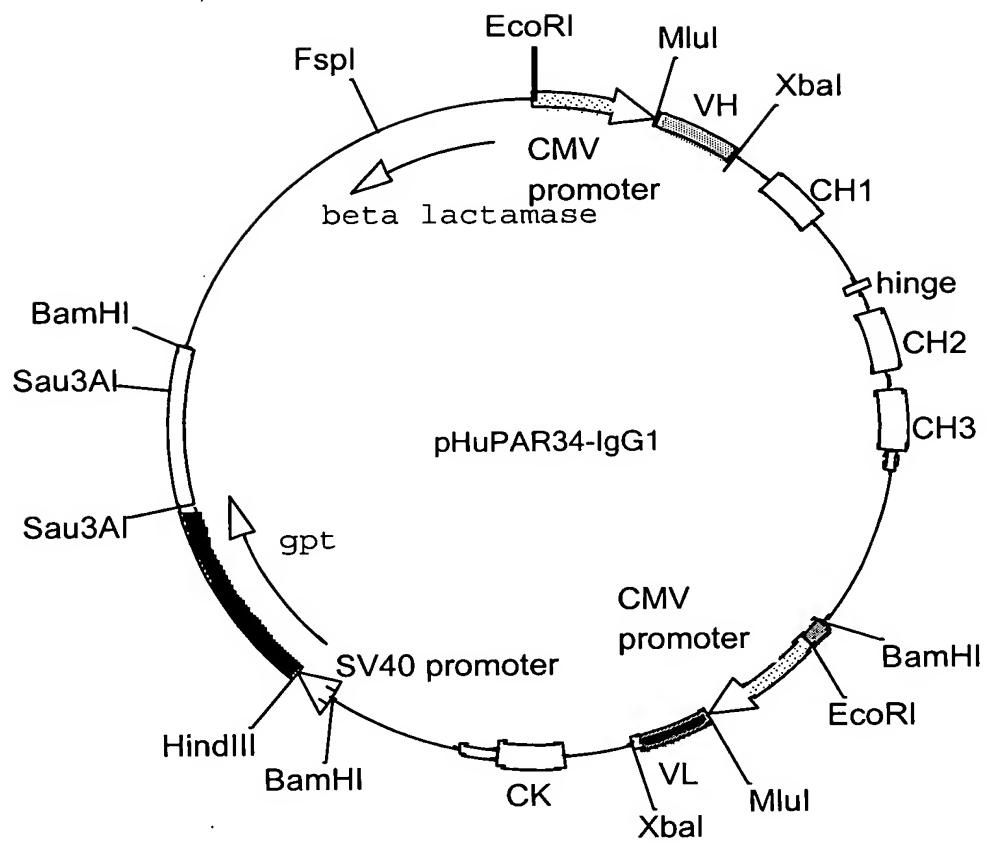


FIG. 17

Binding of Biotinylated MuPAR34 to Amphiregulin

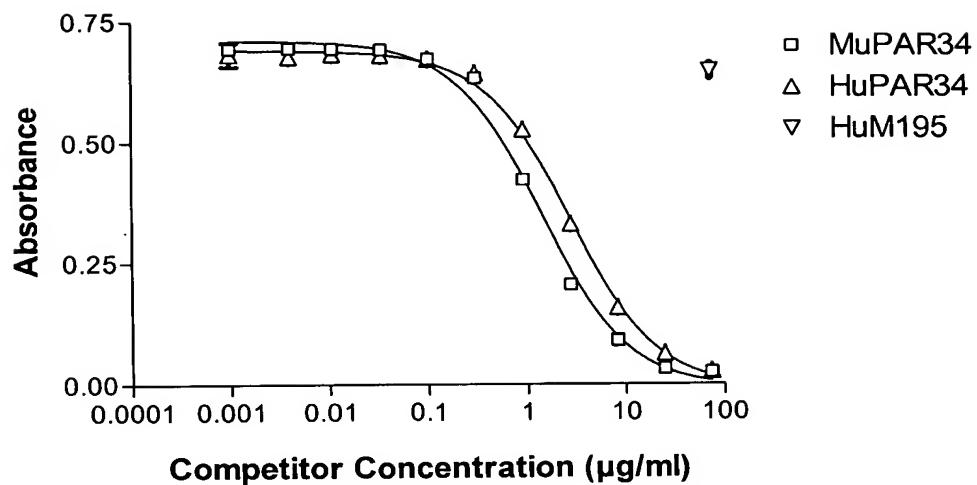


FIG. 18

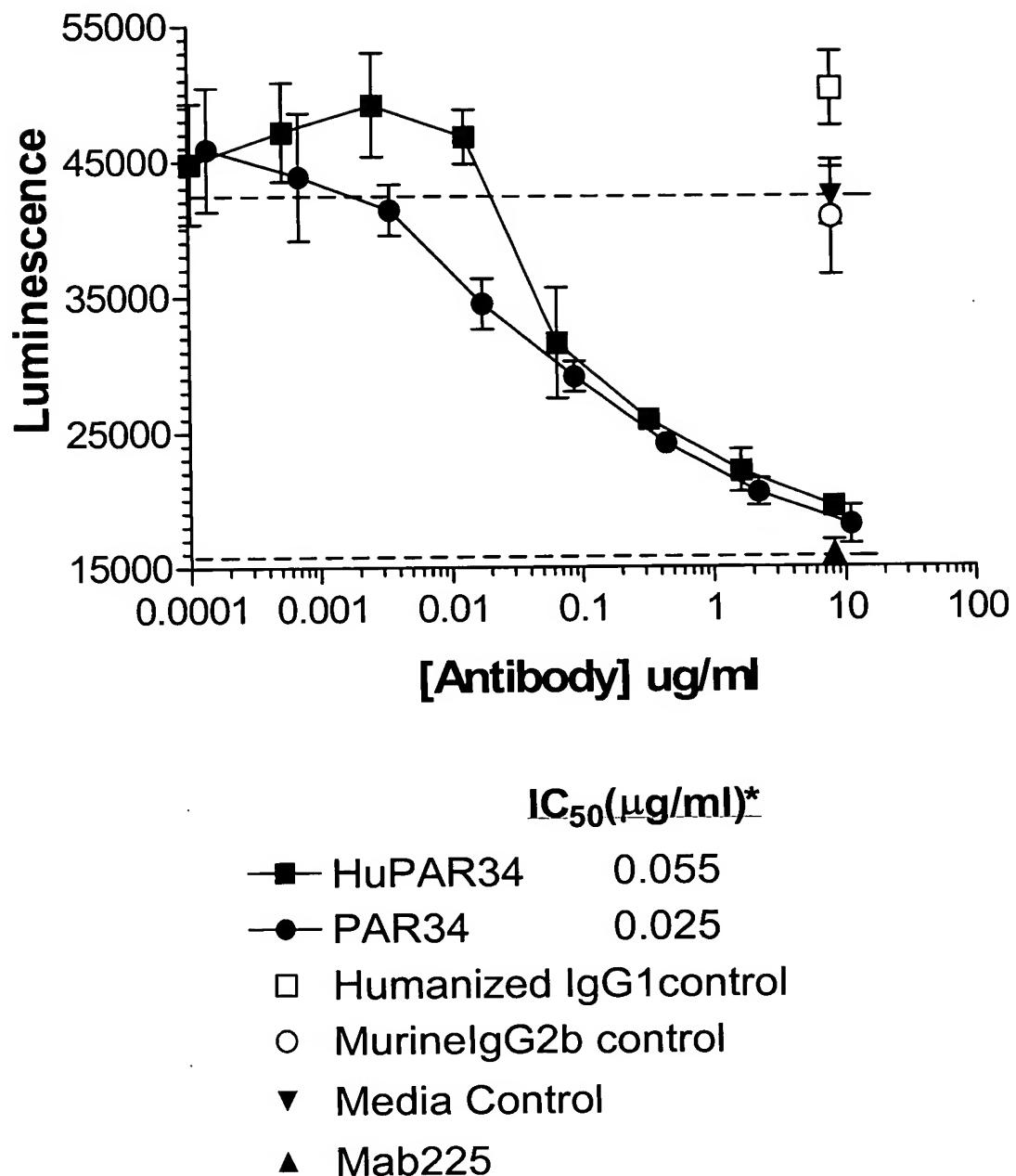
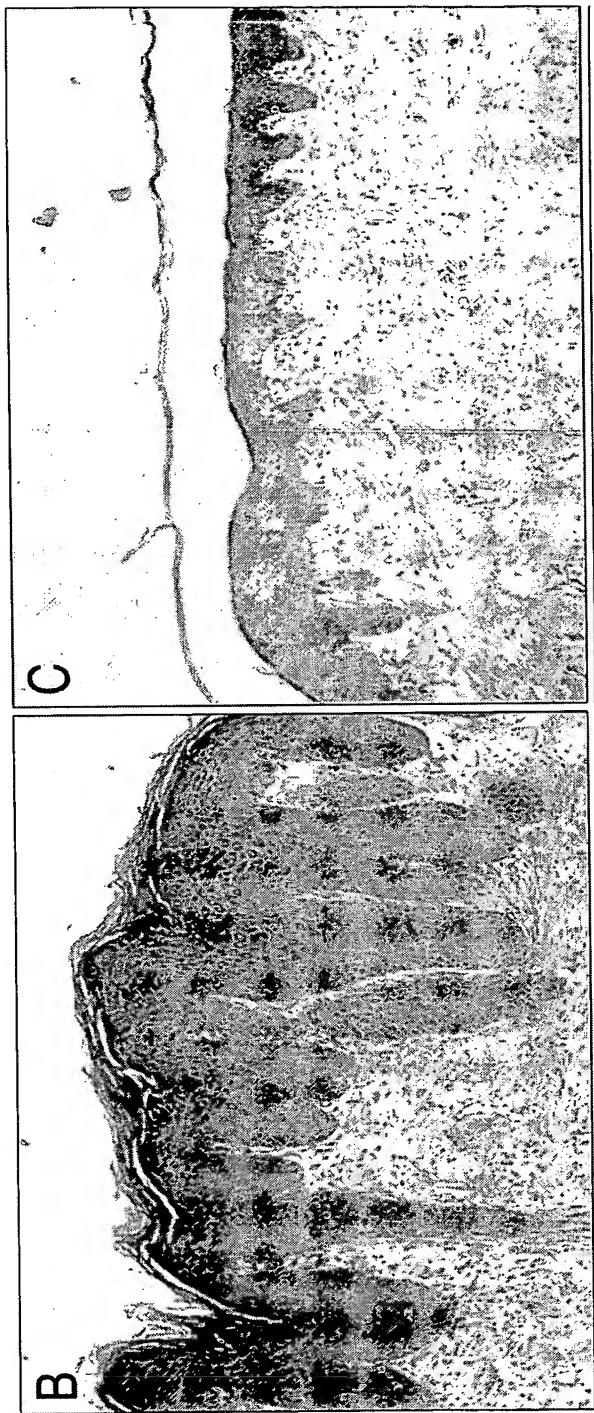


FIG. 19

HUMAN PSORIATIC SKIN/SCID MOUSE TRANSPLANT MODEL
EFFECT OF *HuPAR34* ON NORMAL SKIN GRAFT



**TRANSPLANTED
NORMAL SKIN
+ *HuPAR34***

**TRANSPLANTED
NORMAL SKIN
+ CONTROL ANTIBODY**

FIG. 20

**HUMAN PSORIATIC SKIN/SCID
MOUSE TRANSPLANT MODEL
EFFECT OF *HuPAR34* ON PSORIATIC GRAFT**

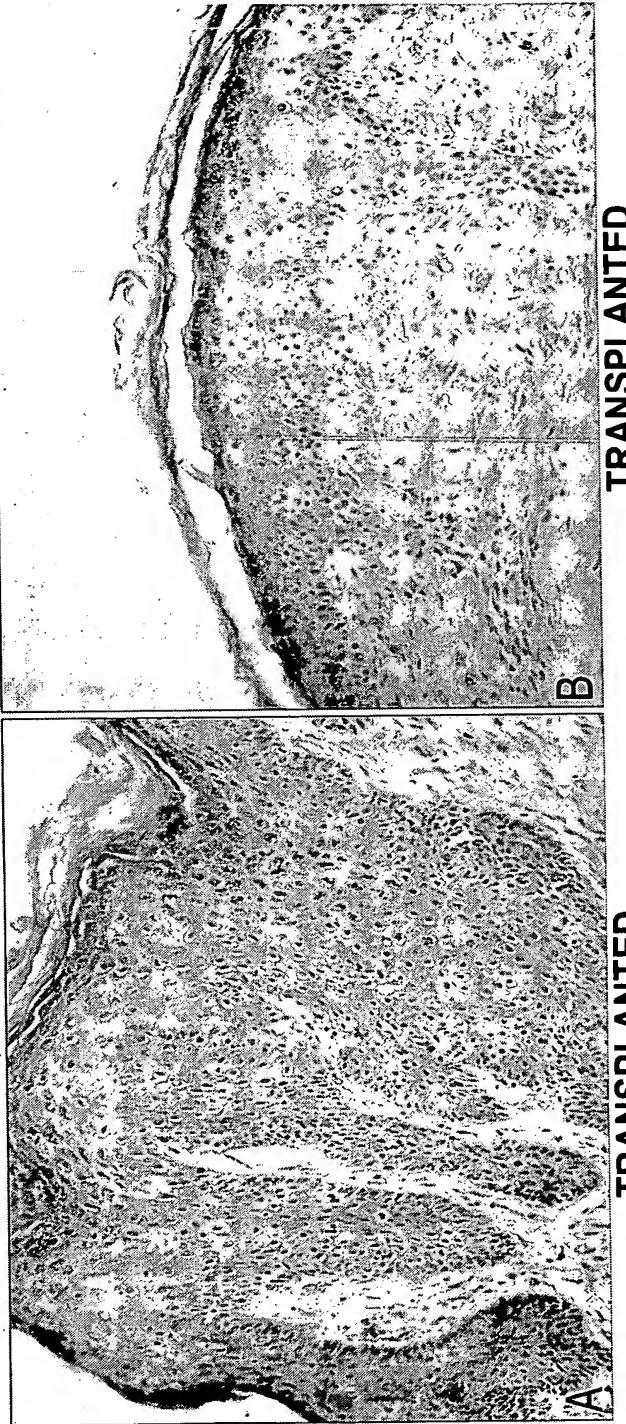
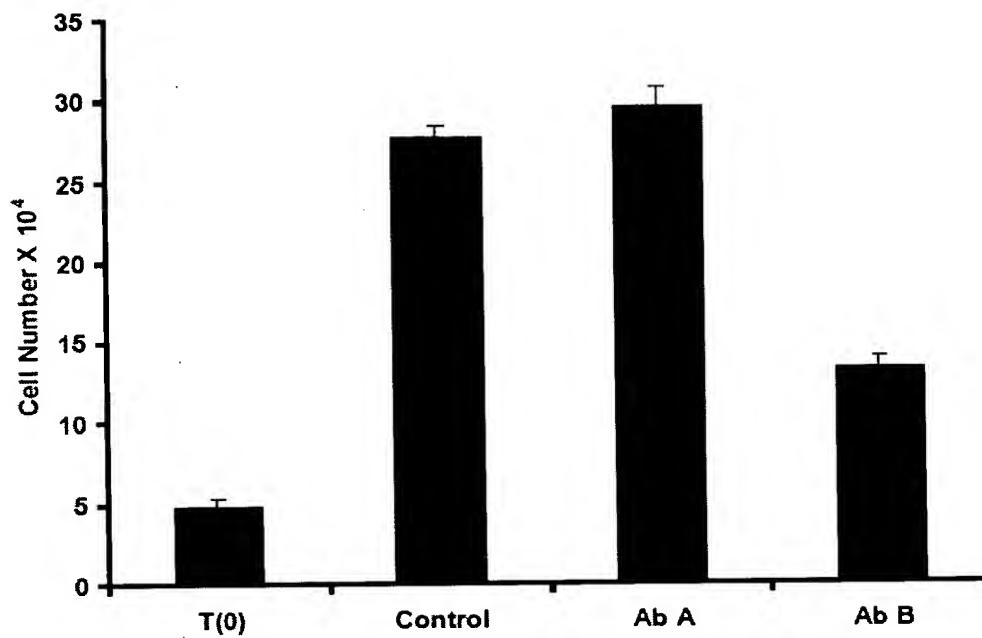


FIG. 21

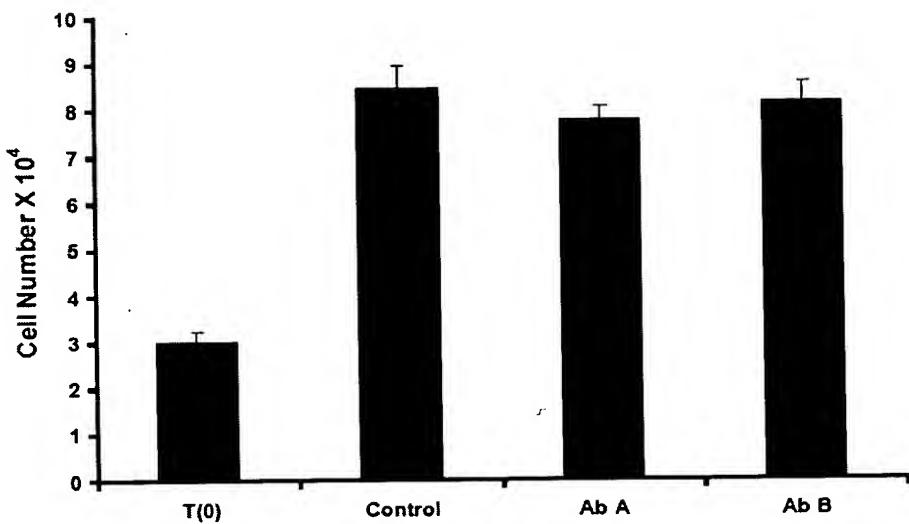
Cell Counts - Keratinocytes



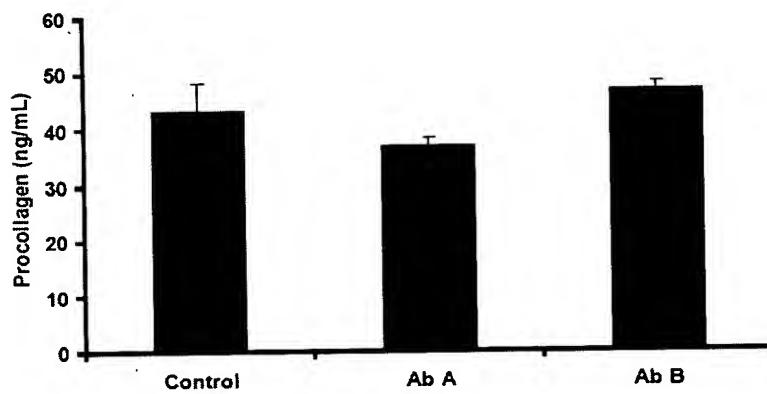
Control:KBM
Ab A: Control Antibody
Ab B: anti-amphiregulin antibody

FIG. 22

Cell Counts - Fibroblasts



Procollagen production - Fibroblasts



Control:KBM

Ab A: Control Antibody

Ab B: anti-amphiregulin antibody

FIG. 23